THE PLASMA PROTEIN EXTRAVASATION INDUCED BY POLISTES LANIO LANIO WASP VENOM IN THE MICE SKIN: INVOLVEMENT OF SENSORY-C FIBERS.

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Stings by *Polistes* sp wasps, found in Brazil, are of clinical interest as they can cause life-threatening allergic reactions, pain and inflammation (Castro *et al.*, 1994). However, little is known about the biological activity and composition of the venom. This study was undertaken to investigate the effects evoked by *Polistes lanio lanio* venom (PLLv) in the cutaneous microvasculature and to identify active inflammatory peptides.

Both male and female C57BL/6 mice (25-30 g) and Wistar rats (200 g) anesthetised with urethane (25% w/v, 100 µl 10 g^{-1}) were used. ^{125}I-albumin (0.03 MBq/0.1 ml) was injected into the tail vein. Intradermal injection (i.d.; 0.05-0.10 ml) of test agents was made into the shaved dorsal skin. Following 30 min period accumulation, animals were killed and skin oedema was assessed via extravascular accumulation of ^{125}I-albumin (Costa *et al.*, 2003). The venom was collected by compressing the venom sac and then was lyophilized and sometimes dialyzed (MW cutoff 2000). The nano-electrospray ionization analysis of venom-containing peptides was carried out via Q-TOF mass spectrometer (Micromass, U.K.) coupled to a CapLC chromatographic system. The MS/MS spectra was processed using MaxEnt3 and sequenced via PepSeq software. PLLv (0.3-30 µg $site^{-1}$) caused a potent and dose-dependent oedema formation into the dorsal skin of mice (not shown; n=3-8). The venom EC_{50} (7 µg)-induced oedema was unaffected by the bradykinin B_2 receptor antagonist HOE 140 (0.8 nmol kg^{-1}; i.v.) but partly reduced by the B_1 receptor antagonist Des-Arg^9-[Leu^8]-BK (3 µmol kg^{-1}, i.v.; 269 ± 28 and 94.5 ± 35* µl $site^{-1}$, control and treated, n=3-4). Dialysis of PLLv reduced the oedema by 50% (Fig. 1). The substance P NK_1 receptor antagonist SR140333, but not NK_2 (SR48968), markedly reduced PLLv-evoked oedema (Fig. 1). Capsaicin treatment to deplete neuropeptides inhibited PLLv-induced response in rats (not shown; n=4). Analysis by mass spectrometry (Q-TOF/CapLC) shows that PLLv contains peptides (MW 1173 – 3581) that share C-terminal sequences with mammalian tachykinins.

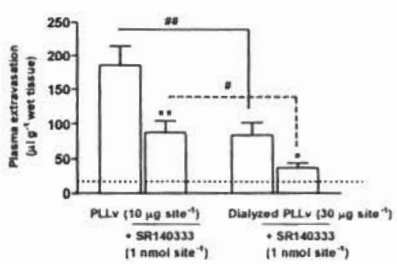

Fig. 1 Effect of raw and dialyzed PLLv in the absence and presence of SR140333 (1 nmol $site^{-1}$; n=7-8) in the mice skin. *$P<0.05$ and **$P<0.01$ vs PLLv without SR140333. #$P<0.05$ and ##$P<0.01$ dialyzed PLLv vs raw venom.

These findings provide new evidence that PLLv-induced inflammatory effect in the skin of rodents is largely mediated by the action of tachykinin-like peptides, in a manner similar to the endogenous neuropeptide Substance P. The venom-induced oedema may also involve activation of BK B_1 receptor in the cutaneous microvasculature.

Castro, F.F.M. *et al.* (1994). *J. Investig. Allergol. Clin. Immunol.*, **4**, 37-41.
Costa, S.K.P. *et al.* (2003). *Br. J. Pharmacol.*, **139**, 59-64.

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